

## **REMARKS**

### **Status of the Claims**

Claims 2 and 4-9 are pending in the present application. Claims 2 and 4 are independent. Claims 4-7 stand withdrawn as being drawn to non-elected inventions.

Claims 1 and 3 were previously cancelled without prejudice or disclaimer of the subject matter contained therein. Claim 1 has been amended and its amendment is at least supported at page 6, lines 16-19 of the Specification as filed.

Reconsideration of this application, as amended, is respectfully requested.

### **Request for Entry of Response After Final Rejection**

This response should be entered after final rejection because it is believed to place the application in condition for allowance.

In the event that the Examiner disagrees and finds that this response does not place this application into condition for allowance, the Examiner is requested to enter this response because it places the application into better condition for appeal.

### **Rejections under 35 U.S.C. §§ 102(b) and 103(a)**

Claim 2 stands rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as being obvious over Yamazawa et al., Polymer Preprints, Japan, Vol. 50, No. 5 (2001), p. 977 (hereinafter "Yamazawa").

Further, claims 8 and 9, which depend from claim 2 also stand rejected, because they do not limit claim 2 in such a way that excludes azobenzene and the prior art is alleged to anticipate the claimed DNA enzymes that bind to azobenzene.

The rejections of claims 2, 8 and 9 are respectfully traversed.

### **1. Location of inserted azobenzene (azobenzene derivatives, spiropyran, or stilbene) in the claimed invention**

In the Office Action, it is asserted that the claims do not recite a substrate binding arm. To clarify that "B" in the formulae represents an end of a substrate binding arm, claim 2 has been amended to specifically recite "an end of sequence of nucleotide or oligonucleotide which is complementary to substrate RNA." This amendment is at least supported at page 6, lines 16-19

of the Specification as filed, where it is stated that "[t]he base sequence of the above-described DNA enzyme except the catalytically active loop is a base complementary to the substrate RNA."

Therefore, the amendment makes clear that azobenzene "X" attached to a structure represented by the formulae in claim 2 is located between an end of catalytically active loop "A" and an end of a sequence complementary to a substrate, that is a substrate binding arm, "B".

In the Office Action, it is also asserted that it is unclear how the azobenzene could be both "within the loop" and "at the junction with [the] binding arm..." Here, the specific structures represented by each of the four formulae recited in the claims, which include azobenzene, are not natural DNA structures. For example, the structure has no nucleobase such as adenine and guanine which is necessary for binding to substrate RNA. Thus, the structure cannot bind to substrate RNA, so that the structure is involved in the loop domain as an end part, not the binding arm. Consequently, the azobenzene is located at the junction between the loop domain and the binding arm, and involved in the loop domain.

## 2. Location of inserted azobenzene as taught by Yamazawa

At page 7 of the Office Action, the phrase "the periphery of [the] boundary" is interpreted as the outermost limit of the boundary between the binding arm and the catalytic loop, based on a definition (provided by the Examiner) of the term "periphery" as the outermost limit of a region or regions. However, the term "periphery" has another definition, "an area lying beyond the strict limits of a thing" (definition from the Merriam-Webster Online Dictionary, <http://www.merriam-webster.com/dictionary/periphery>, attached). Based on this definition, the term "periphery" is interpreted as an area, rather than a limit itself. In view of the definition and the Japanese word in the original Yamazawa reference corresponding to "periphery," the phrase "the periphery of [the] boundary" in the English translation of Yamazawa should be interpreted as "the area around the boundary between the binding arm and the catalytic loop".

Although it is not specifically stated how many nucleotides (or atoms) are included in "the periphery of [the] boundary," Yamazawa clearly teaches that DNA Enzymes 1 and 2 have an azobenzene inserted in "the periphery of [the] boundary", which is not the boundary itself. Additionally, it is clearly described in Yamazawa's experiments that the DNA enzymes were synthesized with the introduction of azobenzene into a substrate-recognition domain, a cleavage-

activity domain, or a base sequence optionally added, where the boundary is not recited. Thus, Yamazawa fails to disclose the introduction of azobenzene into the boundary between the binding arm and the catalytic loop.

Furthermore, Yamazawa fails to disclose how the azobenzene is inserted into the DNA enzyme. For example, it is unclear whether the azobenzene is inserted by addition to the original nucleotide, the replacement of the original nucleotide or introduction between the original nucleotides, and whether the azobenzene is inserted with/without natural nucleotides or non-natural structures. Therefore, Yamazawa neither teaches nor suggests the claimed invention having an azobenzene with a non-natural structure represented by the formulae recited in claim 2 between the binding arm and the catalytic loop.

### 3. Advantages of the claimed invention compared to the DNA enzymes taught by Yamazawa

As discussed in the Amendment filed March 4, 2010 (page 16, lines 11 to 17), DNA-1A, DNA-1B and DNA-1C, which are within the scope of the claimed invention, have a significantly higher RNA cleavage activity (38.8%, 36.0% and 33.3%) than that of a native DNA enzyme (12.5%) (See Table 2), as well as being controlled by irradiation with UV rays (See Table 4 with regard to DNA-1A and DNA-1B).

On the other hand, Yamazawa neither teaches nor suggests such improvements in cleavage activity. Yamazawa only discloses irradiation with UV rays causing the inhibition of RNA cleavage activity by DNA Enzymes 1 and 2 and the increase of RNA cleavage activity by DNA Enzyme 3. Incidentally, Yamazawa's figure shows the ratio of the cleavage activity without UV irradiation (dark) to that with UV irradiation (UV) for each DNA Enzyme. There is no discussion comparing the cleavage activities of Yamazawa's DNA enzymes having azobenzene to native DNA enzymes. Yamazawa fails to disclose the effect of the insertion of azobenzene on the cleavage activity of a DNA enzyme and a DNA enzyme having higher RNA cleavage activity than that of a native DNA enzyme.

One of skill in the art could not simply interpret the DNA enzymes taught by Yamazawa as also having increased cleavage activity (as in the claimed invention), since

(1) there is no specific mention in Yamazawa comparing activity of the experimental DNA enzymes to that of a native DNA enzyme,

(2) azobenzene is not naturally included in DNA and there is no reasonable expectation to improve the cleavage activity by inserting it,

(3) DNA enzymes having azobenzene inserted in the binding arm would reduce cleavage activity, like DNA-2A and DNA-3A in the present application (See Table 4),

(4) in general, the DNA enzymes would be completely intolerant of variation in the loop domain (*e.g.*, Santoro (previously cited) page 4265, last paragraph of left column), and

(5) there is no specific recitation that the DNA enzyme having azobenzene was inserted in the boundary itself, as in the claimed invention.

Therefore, the claimed DNA enzymes having superior RNA cleavage activity are neither anticipated nor obvious over Yamazawa.

In view of the discussion above, Applicants respectfully request that the rejection of claims 2, 8 and 9 be withdrawn.

### **CONCLUSION**

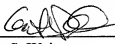
All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Stephanie A. Wardwell, Ph.D., Registration No. 48,025 at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: SEP 15 2010

Respectfully submitted,

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Attachment: definition for "periphery" from the Merriam-Webster Online Dictionary